FDA Patient Safety News: Show #27, May 2004

FDA Approves Two New Drugs for Colorectal Cancer

FDA recently approved two new drugs to treat metastatic colorectal cancer. One is Avastin (bevacizumab) manufactured by Genentech, Inc. and the other is Erbitux (cetuximab), manufactured by ImClone Systems, Inc.

Both of these drugs are monoclonal antibodies, given intravenously, but they work by targeting different proteins. Avastin, an angiogenesis inhibitor, binds to VEGF, or vascular endothelial growth factor, which stimulates the formation of new blood vessels. It's believed that once it's bound, the VEGF is no longer able to stimulate new vessel formation, and this can delay tumor growth.

Erbitux binds to epidermal growth factor receptor (EGFR), a protein that plays a role in regulating cell growth. It's believed that when Erbitux is bound to the receptor, this blocks the epidermal growth factors from binding to the cancer cells, thus blocking their growth.

These two drugs are used as part of different treatment regimens, and at different stages of treatment. Avastin is given as initial treatment for metastatic colon cancer, in combination with the standard three-drug IFL treatment. Erbitux is given to patients whose tumors are no longer responding to standard treatment. It's used with irinotecan, or if patients can't tolerate irinotecan, it's used alone.

In a clinical trial, patients with metastatic colorectal cancer who were treated with Avastin in combination with IFL survived about five months longer than control patients receiving IFL alone. Although treatment with Erbitux has not yet been shown to increase patient survival, it did delay tumor growth, especially when used as a combination treatment.

Treatment with these drugs can cause a range of side effects, some of them serious. For example, rare but serious side effects with Avastin include gastrointestinal perforation, impaired wound healing, hemoptysis and internal bleeding. Erbitux can also cause serious side effects, usually during infusion of the first dose. These can include airway obstruction and hypotension.

Additional Information:

FDA Drug Information Page: Erbitux (cetuximab).
http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm113714.htm

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New Ventricular Assist Device for Children

FDA recently approved a miniaturized ventricular assist device for children ages 5 to 16 who are awaiting a heart transplant. The device, called the DeBakey VAD Child and manufactured by MicroMed Technology, may allow children with severe left ventricular failure to survive long enough to receive the transplant.

While similar ventricular assist devices have been approved for use in adults, this is the first one for children. It was approved under what's called a special Humanitarian Device Exemption, a mechanism through which FDA can make certain devices quickly available on a limited basis for patients with rare medical conditions. It's estimated that fewer than 100 children per year will be candidates for the new device.

Additional Information:

Consumer Information on the DeBakey VAD(r) Child - H030003.
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm081210.htm

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More on Suicidality and Antidepressants

In a previous edition of FDA Patient Safety News, we told you about FDA's ongoing review of a possible increased risk of suicidal thinking and suicide attempts in pediatric patients being treated with various antidepressants.

Although this review is still underway, FDA has now sent a new advisory to health care professionals. The advisory describes new warnings about the need to closely observe both children and adults on antidepressants.

The trade names of the drugs that are the focus of this labeling change include: Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvox (fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and, Remeron (mirtazapine).

The advisory says to carefully monitor patients on these drugs for possible worsening depression or emergent suicidality. This is especially important at the beginning of treatment or when the dose is either increased or decreased.

At this point, a causal link hasn't been established between these drugs and suicidality. Suicidal thoughts and attempts in these patients might be due to the drug, or they could be due to the underlying disease.

Patients who develop suicidal thoughts for the first time when they take these drugs should be carefully monitored to determine whether to discontinue or modify the drug therapy, as should those whose depression becomes persistently worse, or whose suicidality is severe, or abrupt in onset.

The advisory also points out that patients should be observed for anxiety, agitation, panic attacks, and other

behavioral symptoms known to be associated with antidepressant therapy. Although FDA hasn't concluded that these symptoms are a precursor to worsening depression or suicidal impulses, patients who experience these symptoms may be at increased risk. Again, therapy should be evaluated and medications may need to be stopped in patients with symptoms that are severe, abrupt in onset, or weren't part of the patient's presenting symptoms.

Patients and caregivers, including the parents of pediatric patients, also have an important role to play in monitoring. They should be told to look for these kinds of symptoms or suicidal thoughts and report them immediately to health care providers. You can get a copy of FDA's full advisory on our web site.

Additional Information:

FDA Center for Drug Evaluation and Research: Antidepressant Use in Children, Adolescents and Adults.
http://www.fda.gov/cder/drug/antidepressants/default.htm

Recall of Faulty Patient Lifts

FDA recently announced that certain battery-operated patient lifts are being recalled by their distributor because they can break during use and endanger patients. The lift in question is called the Faaborg Person Lift. It's manufactured in Denmark and distributed in the U.S. by Moving Solutions. Over 800 of these lifts have been sold in this country.

The problem occurs when the bolt that secures the hanger bar to the lift arm bar breaks. This can cause the patient to fall, and possibly cause the hanger bar to fall on the patient as well. One death has been reported because of this failure in the bolt.

In January, Moving Solutions notified users of the problem and included a nylon washer to be inserted over the bolt. At this point, FDA is investigating whether the washer will correct the problem. In the meantime, FDA is advising all facilities that have Faaborg battery operated Person Lifts to stop using them.

Additional Information:

Medical Device Recalls. Class 1 Recall: Faaborg Patient Lifts.
http://www.fda.gov/MedicalDevices/Safety/RecallsCorrectionsRemovals/ListofRecalls/ucm064843.htm

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Recall of Certain Nasal Decongestants

Major Pharmaceuticals, a drug distributor, is recalling certain lots of the company's OTC nasal decongestant. Some of the recalled lots are contaminated with Burkholderia cepacia, which could cause potentially life-threatening infections when used by patients with compromised immune systems, particularly those with cystic fibrosis.

The recalled spray is sold over-the-counter in 15 and 30 ml bottles. The label says "Major Soothing Twice-A-Day 12 Hour Nasal Spray Decongestant, Regular Oxymetazoline Hydrochloride 0.05%. Distributed by Major Pharmaceuticals, Livonia, MI".

Ten lots of this product are currently being recalled: E4410, F4433, H4464, K4496, L4529, L4535, M4536, A4558, A4588, and B4597. If you stock this product, or have patients who use it, look for the lot number on the bottom of the carton and on the back of the bottle label. You can find additional information and instructions on how to return the recalled product on our web site.

Additional Information:

Recall - Firm Press Release: Major Twice-A-Day 12 Hour Nasal Spray.
http://www.fda.gov/Safety/Recalls/ArchiveRecalls/2004/ucm111576.htm

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Dangerous Mixups Between Opium Tincture and Paregoric

Recent articles have warned health professionals about dangerous mixups between opium tincture and paregoric. Since 1997, FDA has received eight reports of medication errors involving these two drugs. Three were fatal, and three others required medical treatment.

The danger stems from the fact that opium tincture is 25 times more concentrated than paregoric. So if the practitioner thinks he or she is ordering paregoric, but is actually ordering opium tincture, the patient can receive a large overdose.

Although the two names don't sound alike, these two drugs each have several synonyms, and it's those synonyms that can easily be confused.

Opium tincture is also called deodorized opium tincture, deodorized tincture of opium, tincture of opium, laudanum, opium, and DTO, which is an abbreviation for "deodorized tincture of opium."

Paregoric is also called camphorated tincture of opium and tincture of paregoric. So you can see how this confusion of names can lead to errors.

For example, some practitioners have prescribed "DTO" thinking that this abbreviation stands for "diluted tincture of opium," when it actually means "deodorized tincture of opium." As a result, patients have been seriously overdosed.

To help resolve the confusion, FDA will be working with the manufacturers of these two drugs to clarify the labeling on the containers and in the package inserts. In the meantime, it's important to educate staff members about possible confusion between the two products.

One general rule of thumb that can help to prevent errors is to remember that opium tincture is dosed in drops, in other words in fractions of a milliliter, whereas paregoric is dosed in teaspoons. So any order for opium tincture that specifies teaspoonful doses is likely to be in error.

Our web site lists a number of additional recommendations to avoid mixups between paregoric and opium tincture that hospital pharmacies might want to consider. Here are a few of them.

First of all, determine if there's a need to even stock opium tincture. Check the last time this medication was dispensed, and eliminate it from the inventory if possible.

If you're going to stock both products, be sure to keep the terminology clear and consistent. Call paregoric "paregoric," and not "camphorated tincture of opium." And call opium tincture "opium tincture," and not "DTO."

Put poison labels on all containers of opium tincture, as well as a label stating the strength of morphine per mL, and a statement such as "WARNING! Do NOT confuse opium tincture with paregoric."

Since accurately measuring opium tincture doses can be difficult, consider dispensing it only in small dropper

bottles or oral syringes.

Additional Information:

Drug Topics (July 7, 2003). FDA Safety Page: Drug errors associated with opium tincture and paregoric.

http://www.fda.gov/cder/drug/MedErrors/opiumTincture_paregoric.pdf

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Teaching Patients to Use EPIPEN

Millions of people have severe allergies to food, insect venom, drugs, latex, or other allergens. Many of these patients are given epinephrine autoinjectors such as EpiPen to use when an anaphylactic reaction occurs.

But patients may not always be well trained on how to use these devices, or they may not remember what to do in an emergency. So here's a quick step-by step review of how to use one widely prescribed brand of injectable epinephrine - the EpiPen, distributed by DEY. You may want to pass this information on to your patients with severe allergies.

Remove the EpiPen from its amber tube. Grasp it with the thumb towards the gray activation cap, but not over it. Remove the cap. Be sure not to touch the black tip at the other end of the EpiPen once the cap is removed. Hold the autoinjector with the black tip towards the outer thigh. Swing and jab firmly at a 90 degree angle into the outer thigh. Keep it against the thigh for 5 -10 seconds. Remove the EpiPen and massage the injection site for several seconds. Look at the tip to be sure the needle is visible. And check the small clear window on the EpiPen for the black plunger, indicating that the epinephrine has been injected.

After using the EpiPen, press the needle against a hard surface to bend it back towards the shaft. Then return it to the amber tube. Call 911 and go to an emergency room as soon as possible. Patients should take the used EpiPen with them to the hospital and give it to the physician for inspection and for proper disposal.

For EpiPen Educational Materials, call 1-800-755-5560

Additional Information:

EpiPen Web Site.
http://www.epipen.com

Caution on Neurological Damage from Absorbable Hemostatic Agents

FDA has issued a Public Health Notification reminding surgeons that absorbable hemostatic agents can cause neurological damage if they're applied on or near a bony or neural space and left in the patient. Since 1996, FDA has received more than 100 reports of adverse events with absorbable hemostatic agents, eleven of which resulted in paralysis or other neural deficits.

The common thread in all eleven incidents was that the absorbable hemostatic agent was applied on or near a bony or neural space and left in the patient.

Once it was wet, the material swelled and then exerted pressure on the spinal cord or other neural structures. In some cases, blood pooled behind the material and formed a hematoma that exerted pressure on neural

tissue.

Although these events are rare, they can have grave consequences. And they're largely preventable.

The Notification recommends two specific steps to reduce the risk. First, when you're using an absorbable hemostatic agent on or near bony or neural spaces, use only the minimum amount necessary to achieve hemostasis. And second, remove as much of the material as possible after hemostasis is achieved.

Additional Information:

MedWatch 2004 Safety Summary: Absorbable Hemostatic Agents.
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm155625.htm

Warning about ZYPREXA (olanzapine)

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Now a warning about the drug ZYPREXA (olanzapine), made by Eli Lilly and company. ZYPREXA is used to treat schizophrenia and bipolar disorder.

The WARNINGS section of the drug's label now describes cerebrovascular adverse events. These have occurred in elderly patients being treated for dementia-related psychosis in clinical trials. These events, some of them fatal, have included stroke and TIAs. The labeling reminds practitioners that ZYPREXA has not been approved for the treatment of patients with dementia-related psychosis.
